REMARKS

Claims 20, 23-28, 31-44, 50, 64-68 and 89-92 are pending. Claims 93-107 are new. Support for claims 93-100 is found, for example, in the specification at page 46, line 8 – page 47, line 11, and in the process of Figure 4. Support for claims 101-107 is found, for example, in the specification at page 47, line 12 – page 48, line 4, and in the process of Figure 5.

Claims 20, 23-28, 31-44, 50, 64-68 and 89-92 stand rejected. Applicants respectfully request reconsideration of the pending rejections based on the following comments.

Claims Rejections under 35 U.S.C. § 103

The Examiner has maintained the rejection of claims 20, 23-28, 31-44, 50, 64-68 and 89-92 under 35 U.S.C. § 103(a) as allegedly obvious over BeMiller, *et al.* ("BeMiller") in view of the Merck Index ("Merck"), Sundberg, *et al.* ("Sundberg"), McFarlin, *et al.* ("McFarlin") and Piccirilli, *et al.* ("Piccirilli"). The Examiner alleges that the instant claims are obvious because BeMiller teaches the conversion of D-fructose to 2-C-methyl-D-ribonolactone with aqueous calcium hydroxide, Merck teaches that CaO in water forms aqueous calcium hydroxide, Sundberg teaches that an alkoxyaluminum hydride reagent can be used to reduce a lactone carbonyl group to an alcohol, McFarlin teaches that $LiAl(O^tBu)_3H$ is a mild reducing agent, and Piccirilli teaches that certain ribose sugars are synthetic targets for potential therapeutics. (Office Action, pages 4-7). Applicants respectfully disagree.

First, the Examiner alleges that the first step of the instant claims, adding CaO to a solution of D-fructose, is obvious merely because BeMiller teaches the reaction of aqueous calcium hydroxide with D-fructose, and Merck teaches that adding CaO to water generates aqueous calcium hydroxide. (Office Action, page 5). To make a *prima facie* case of obviousness, the Examiner must "*identify a reason* that would have prompted a person of ordinary skill...to combine the elements in the way the claimed new invention does." *KSR International Co. v. Teleflex Inc.* 82 U.S.P.Q.2d 1385, 1395 (2007) (emphasis added). The Examiner merely alleges that one skilled in the art would "readily recognize" that reacting CaO with a solution of fructose would be equivalent to the reaction of BeMiller. (Office Action, page 5). The Examiner has provided no *reason* why one skilled in the art would modify the process of BeMiller to use the specific step of adding CaO to a solution of D-fructose as recited in the instant claims. The process of BeMiller works for its intended purpose– the conversion of fructose to 2-C-methyl-D-ribonolactone– without the use of CaO. Thus, there is no motivation

to replace aqueous calcium hydroxide with CaO. The mere fact that one skilled in the art would "recognize" that CaO forms calcium hydroxide in water does not create a motivation to modify the process of BeMiller to use CaO in a specific step as recited in the instant claims. Without such a motivation, the Examiner has not made a *prima facie* case of obviousness.

The Examiner has also failed to demonstrate that one skilled in the art would be motivated to arrive at the third step of the process of the instant claims. The Examiner alleges that one skilled in the art would be motivated to substitute $LiAlH_2(OCH_2CH_2OCH_3)_2$ for $LiAl(O^tBu)_3H$ to arrive at the process of step 3 of the instant claims. (Office Action, page 5). The Examiner bases this alleged motivation on the structural similarity of the two hydride reagents. *Id.* However, one skilled in the art would recognize that while $LiAlH_2(OCH_2CH_2OCH_3)_2$ and $LiAl(O^tBu)_3H$ are structurally similar, they have different reactivities. Indeed, Sundberg, the reference cited by the Examiner, teaches that $LiAlH_2(OCH_2CH_2OCH_3)_2$ may be used to reduce lactones to lactols, but is silent regarding the use of $LiAl(O^tBu)_3H$ in this regard. (Sundberg, page 236). Moreover, Sundberg also teaches that the reduction of esters is slower in the case of $LiAl(O^tBu)_3H$. *Id.*

Indeed, the instant claims are not obvious over the references cited by the Examiner because Sundberg teaches away from the use of $LiAl(O^tBu)_3H$ in place of $LiAlH_2(OCH_2CH_2OCH_3)_2$ for the claimed process. "An applicant may rebut a *prima facie* case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." *In re Peterson,* 315 F.3d 1325, 1331, 65 USPQ2d 1379 (Fed. Cir. 2003)(citing *In re Geisler,* 116 F.3d 1465, 1469, 43 U.S.P.Q.2d 1362 (Fed. Cir. 1997)). To demonstrate the reduction of a lactone to a lactol, Sundberg teaches the use of $LiAlH_2(OCH_2CH_2OCH_3)_2$ as the reducing agent, not $LiAl(O^tBu)_3H$. (Sundberg, page 236). Sundberg also teaches that the reduction of esters to alcohols is slow when using $LiAl(O^tBu)_3H$, but not when $LiAlH_2(OCH_2CH_2OCH_3)_2$ is used. *Id.* In this regard, Sundberg teaches away from the use of $LiAl(O^tBu)_3H$ to reduce a lactone to a lactol because a lactone is a cyclic ester, and Sundberg teaches that the reduction of esters is slow with $LiAl(O^tBu)_3H$. Contrary to what the Examiner alleges, one skilled in the art, reading Sundberg, would not be motivated to select $LiAl(O^tBu)_3H$, the weaker reagent.[1] Therefore, step 3 of the process of the instant claims is not obvious over Sundberg.

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[1] The Examiner alleges that one skilled in the art "would want to choose the milder [reagent] since it would not cause other side reactions...." (Office Action, page 6). To the contrary, as Sundberg

The Examiner also alleges that the teachings of McFarlin provide motivation to use $LiAl(O^tBu)_3H$ in the process of the instant claims. (Office Action, page 6). To the contrary, McFarlin also teaches away from the use of $LiAl(O^tBu)_3H$ in the process of the instant claims. First, McFarlin does not teach the reduction of esters or lactones with $LiAl(O^tBu)_3H$. Indeed, of the examples provided in McFarlin, the only reduction of an ester attempted with $LiAl(O^tBu)_3H$ failed. (McFarlin, Table II, page 5373). Therefore, one skilled in the art, reading McFarlin, would have no motivation to select $LiAl(O^tBu)_3H$ for the reduction of a lactone as recited in the instant claims.[2]

Furthermore, the Examiner has failed to make a case of *prima facie* obviousness because he has disregarded an essentail step in the analysis– a showing that one skilled in the art "would have perceived a reasonable expectation of success in making" the claimed invention by combining the teachings of BeMiller, Merck, Sundberg, McFarlin and Piccirilli. *Medichem v. Robaldo*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (*citing In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988). While an Examiner may properly base an obviousness rejection on the teaching, suggestion, or motivation rationale, part of that analysis requires the showing of a reasonable expectation if success. *See* Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, 72 Fed. Reg. 57,526, 57,528 (Oct. 10, 2007); *see also KSR*, 82 U.S.P.Q.2d at 1396. The Examiner has not demonstrated that one skilled in the art would have had a reasonable expectation of success in practicing the process of the instant claims by combining the teachings of BeMiller, Merck, Sundberg, McFarlin and Piccirilli. Therefore, the Examiner has failed to state a *prima facie* case of obviousness.

Finally, the Examiner cites a line of cases allegely holding that the use of a different starting material in a known or conventional process does not render that process nonobvious. (Office Action, page 5). However, as demonstrated above, this is not a case of changing starting materials in a known process, but a case of a new, nonobvious process using reagents in a multi-step process not taught or suggested by the references cited by the Examiner. Furthermore, two

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teaches, the milder $LiAl(O^tBu)_3H$ is shown to slowly reduce esters to alcohols, which would appear to be undesirable in the instant process.

[2] The Examiner cites Piccirilli only to allege that certain ribose sugars are synthetic targets for potential therapeutics. (Office Action, page 6). The Examiner does not maintain that Piccirilli provides any motivation to use CaO or $LiAl(O^tBu)_3H$ in the claimed process, therefore, Applicants maintain that Piccirilli adds nothing to the Examiner's *prima facie* case of obviousness.

of the references cited by the Examiner teach away from the instant process. For at least these reasons, the instant claims are nonobvious over BeMiller in view of Merck, Sundberg, McFarlin and Piccirilli. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Obviousness-Type Double Patenting Rejection

Claims 20-28, 36, 50 and 64-67 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims 1-2 of U.S. Patent Application No. 10/882,893. Applicants respectfully request that this rejection be held in abeyance while the above rejection under 35 U.S.C. § 103(a) is resolved. However, upon resolution of the remaining rejection, Applicants respectfully request reconsideration of the obviousness-type double patenting rejection based on the following remarks.

If provisional obviousness-type double patenting rejections are the only rejections remaining in an earlier filed pending application, the Examiner should withdraw those rejections and permit the earlier-filed application to issue as a patent without a Terminal Disclaimer. Manual of Patent Examination Procedure § 804, subsection I.B.

The filing date of the instant application is December 12, 2003. The filing date of U.S. Patent Application No. 10/882,893 is June 30, 2004. Therefore, because the instant application is the earlier-filed application, and only the provisional obviousness-type double patenting rejection remains, Applicants respectfully request that the Examiner withdraw the rejection and allow the instant application to issue as a patent without a Terminal Disclaimer.

CONCLUSION

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

Please apply fees for a Request for Continued Examination ($810.00) and any other charges, or any credits, to Jones Day Deposit Account No. 503013 (ref. no. 417451-999027).

If the Examiner believes it would be useful to advance prosecution, the Examiner is invited to telephone the undersigned at (858) 314-1200.

Respectfully submitted,

Date: October 30, 2007

Dale Rieger Reg. No. 43,045

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